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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/069,692	06/07/2002	Clifford Smith	PA-9943	3742

22840 7590 04/06/2004

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PATENT DEPARTMENT
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EXAMINER
MCINTOSH III, TRAVISS C

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 04/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/069,692	SMITH ET AL.	
	Examiner	Art Unit	
	Traviss C McIntosh	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/21/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Examiner of the U.S. Patent application SN 10/069,692 has changed. In order to expedite the correlation of papers with the application please direct all future correspondence to the Technology Center 1600, Art Unit 1623, attn: Examiner Traviss McIntosh.

The Amendment filed October 30, 2003 has been received, entered into the record, and carefully considered. The following information provided in the amendment affects the instant application by:

- Claims 10-15 have been withdrawn.

Remarks drawn to rejections of Office Action mailed July 25, 2003 include:

Arguments regarding the restriction requirement.

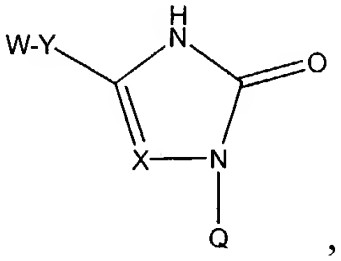
An action on the merits of claims 1-9 is contained herein below.

The text of those sections of Title 35, US Code which are not included in this action can be found in a prior Office action.

Election/Restrictions

Applicant's election with traverse of Group I in Paper No. 10/30/2003 is acknowledged. The traversal is on the ground(s) that the restriction is improper since all the groups contain the same technical feature as having (the core) modified by various side chains. This is not found persuasive because PCT Rule 13.2 requires that unity of invention exists only when the shared same or corresponding technical feature is a contribution over the prior art. Section (f)(i)(B)(1)

of Annex B of the Administrative Instructions requires that all alternatives of a Markush Group have a common structure. Although chemical compounds of claims 1-9 share a common structure of the following:



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the compounds are not regarded as being of similar nature because the shared common structure is not a contribution over the prior art, as Fukuda et al. (cited in the prior office action) discloses compounds having the same core structure as the compound above.

Applicants additionally argue that Groups V, IX, and XIII all contain the structures of Group I, and thus share a common technical feature. The examiner agrees with applicants on this, and thus the examiner will examine Groups V, IX, and XIII together with Group I, inasmuch as Groups V, IX, and XIII read on Group I. That is, Groups V, IX, and XIII will be examined as they apply to the elected invention of Group I. Thus, claims 10-15 are being examined with claims 1-9 as they read upon the election of Group I.

The requirement is still deemed proper and is therefore made FINAL.

Double Patenting

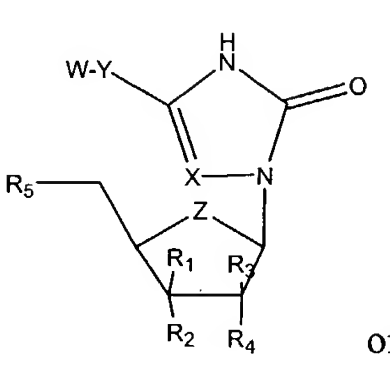
The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

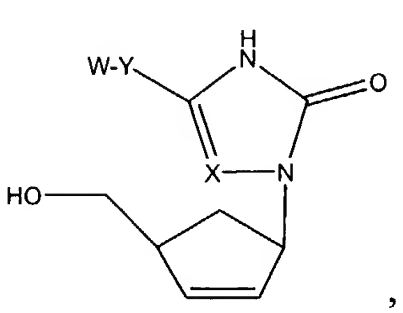
Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-15 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 6,239,159 in view of Fukuda et al. (reference C1 of IDS).

Claims 1 and 2 of the instant application are drawn to a compound represented by one of the following structures:



or



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wherein:

X is: either CH or N;

Y is optionally: -CO-, -CONW-, -O-, -S-, -SO-, -SO_2-, -NWCO-, -NW-, or –OCO-;

W is optionally: H, alkyl, aryl, Rp, or –Ln-Rp;

Ln is a linker group;

Rp is a reporter moiety;

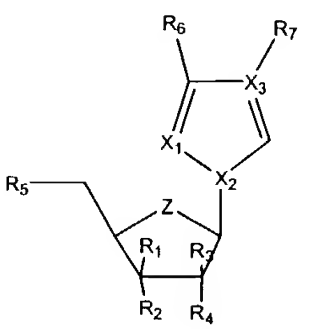
Z is: O, S, Se, SO, NW, or CH_2;

R^1, R^2, R^3, and R^4 are optionally: H, OH, F, NH_2, mono-, di-, or tri-phosphate, -thiophosphate, or –boranophosphate;

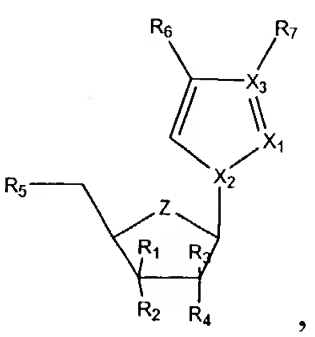
or one of R^2 and R^5 is a phosphoramidite or other group for incorporation in a polynucleotide chain, or a reporter moiety.

Claim 3 provides that Rp is not in the sugar portion. Claim 4 provides that the linker group is a chain of 1-60 C, N, O, P, and/or S atoms, is rigid or flexible, or is saturated or unsaturated. Claim 5 and 6 provide that the reporter moiety is a signal moiety or a solid surface or a group (NH_2, OH, COOH, $CONH_2$, ONH_2, SH, a thiophosphate, hydrazine, hydrazide, an active ester, aldehyde, or maleimide) which can link to a signal moiety or solid surface. Claim 7 is drawn to a nucleoside comprising the compound of claim 1. Claim 8 is drawn to a nucleotide comprising the compound of claim 2. Claim 9 limits the R^5 group of claim 8 to triphosphate. Claim 10 is drawn to a polynucleotide chain comprising the nucleoside of claim 7. Claim 11 limits the polynucleotide of claim 10 wherein the sugar is a nucleic acid backbone consisting of sugar-phosphate repeats or modified sugar-phosphate repeats, or a backbone analogue. Claims 11 and 12 are drawn to chain extension methods comprising reacting the polynucleotide chain of claim 10 with a primer in the presence of a polymerase. Claims 14 and 15 are drawn to methods of detecting a nucleic acid of claim 1 comprising the steps of detecting the presence of the reporter moiety (wherein the reporter is a radioisotope, isotope, signal moiety, or moiety detectable by spectroscopy).

The '159 patent is drawn to nucleosides optionally having the following structure:



or



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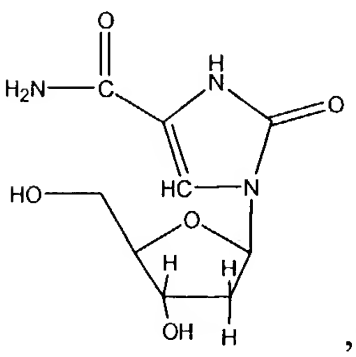
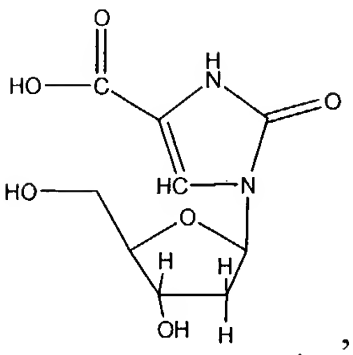
wherein Z, R_1, R_2, R_3, R_4, R_5, R_6, and R_7 are drawn to multiple groups which overlap substantially with the corresponding R-groups of the instant application. X_1, X_2, and X_3 are optionally C or N. The main structural difference between the compounds above and the compounds as claimed in the instant application is the inclusion of 2 double bonds in the base portion of the nucleoside (between X_3 and X_1 in the second structure, for example). The '159 patent additionally claims that the reporter group can be attached via a linker group (claim 6). Claims 7 and 8 are drawn to polynucleotide chains containing the nucleoside of claim 1 and a signal moiety. Claims 9 and 10 are drawn to chain extension methods comprising reacting the polynucleotide chain of claim 10 with a primer in the presence of a polymerase, for example. Claim 11 is drawn to a method of detecting a nucleic acid of claim 1 comprising the steps using an antibody which binds to the base (which comprises a reporter moiety). What is not specifically taught is the compounds of the instant application, or the use of the compounds of the instant application.

Fukuda et al. disclose compounds having the following structure :



, which falls within the group of compounds claimed in the instant application wherein X=CH, Z=O, Y=CO, W=Rp=NH_2, R^1=R^3=R^4=R^5=H, and R^2=OH (see compound 1, page 1572). Fukuda et al. additionally disclose the following compound:



, which falls within the group of compounds as claimed in the instant application wherein X=CH, Z=O, Y=CO, W=Rp=OH, R^1=R^3=R^4=H, and R^2=OH (see compound 3, page 1572). Moreover, compound 5 of Fukuda et al. is drawn to an active ester of the compound 3. Additionally, compound 15 (page 1573) comprises a phosphorylated 2'-deoxynucleotide of the compound of formula 1. Additionally, Fukuda et al. disclose that the compounds of formula 15 were applied to solid phase oligomer synthesis by phosphotriester method (page 1573, 1st column, 1st paragraph). Moreover, table I on page 1574 discloses polynucleotides comprising the nucleoside analogue X (which is analogue 1 as evidenced on page 1573, 2nd column, 1st paragraph). The compounds of Fukuda were designed to be heterocyclic "lure" bases which, when incorporated into ambiguous positions of oligo-deoxynucleotide probe, were expected to contribute to the stabilization of the duplex by pairing with natural base counterparts (page 1571, 2nd column). Compound 1 of Fukuda et al. is shown to be a common substitute for T and C at the position of redundancy, and are therefor shown to be good analogues for binding to pyrimidine bases (page 1574, second column). Thus, the compounds as claimed in the instant application are known in the art to be art recognized nucleoside analogues.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the nucleoside analogues of Fukuda et al. and add various signal moieties on them for detection in a polynucleotide as in the '159 patent with these references before them. Fukuda et

al. shows that their compounds are indeed effective as nucleoside analogues, and that they bind with pyrimidine bases in duplex DNA sequences. The '159 patent is drawn to compounds with reporter molecules which are to be included into duplex DNA sequences, and then later to be detected via the reporter group, thus it would have been obvious to use the compounds of Fukuda et al. because they were already known to be capable of being incorporated into DNA sequences. Moreover, obviousness based on similarity of structure and function entails motivation to make claimed compound in the expectation that compounds similar in structure will have similar properties. Where the prior art compounds essentially bracket the claimed compounds and are known to be effective as well known pesticides, for example, one of ordinary skill in the art would be motivated to make the claimed compounds in searching for new pesticides. See ***In re Payne, 606 F.2d 303, 203 USPQ 245, 254-55 (CCPA 1979).*** As evidenced supra, the compounds of the instant application and the compounds of the '159 patent are indeed very similar in structure, wherein the compounds of '159 have an additional double bond, and have different locations for various overlapping substituents on the ring.

Claims 1-15 of the instant application are seen to be obvious over claims 1-12 of '159, when seen in light of the Fukuda et al. reference.

Claim Objections

Claim 2 is objected to because of the following informalities: the claim does not end in a period. Appropriate correction is required.

Claim 13 is objected to because of the following informalities: the claim has a misspelling in line 2, wherein it is believed applicants intended "hybridize" instead of "hybrisise". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is drawn to a compound wherein Ln is a linker group and Rp is a reporter moiety, which is seen to be missing a critical element. The claim fails to particularly point out the identity of the compound instantly claimed. The current claim language is drawn to a compound which is not described structurally/formulaically/nomenclatorially; but rather by the different variables mode of action, function or effect requisite to an activity produced by the compounds different variables. The claim is missing the critical element, which is the particular or distinct identity of the variables on the compound. Defining the variables structurally, formulaically, or nomenclatorially would be a more preferable way to define the subject matter instead of the current functional description.

Additionally, claim 1 also comprises the phrases "sugar analogue" and "backbone analogue". It is noted that while this portion of the claim is not being taken into consideration, as the restriction requirement set forth groups with defined sugars, the examiner would like to note

that the use of phrases such as "sugar analogue" and "backbone analogue" in a claim, without further definition included therein, would render the claim in which they are contained indefinite. It is unclear as to what would be intended by a "sugar analogue" or a "backbone analogue".

Claim 2 is indefinite wherein the claim defines one of R^2 and R^5 as "a phosphoramidite or other group for incorporation in a polynucleotide chain, or a reporter moiety". It is unclear as to what "another group for incorporation in a polynucleotide chain" is intended to be, as enough modifications could technically allow any molecule or group to be incorporated in a polynucleotide chain. Additionally, the phrase "reporter moiety" is indefinite for the reasons set forth supra.

Claim 3 is indefinite wherein the claim states that "a reporter moiety is not present in Q". However, claim 5 provides that the reporter moiety can be a reactive group, and claim 6 provides that the reactive group is optionally OH. How can the Q molecule not have OH, as it is disclosed as comprising hydroxy groups.

Claim 4 is indefinite wherein the Markush group is confusing. The claim currently reads as "the linker group Ln is a chain of 1-60 C, N, O, P, and/or S atoms, rigid or flexible, saturated or unsaturated". Markush language must be in the alternative form, thus it is noted that the examiner has interpreted the claim as the following: "the linker group Ln is a chain of 1-60 C, N, O, P, and/or S atoms, **or** is rigid or flexible, **or** is saturated or unsaturated".

The phrase "signal moiety" in claim 5 is indefinite. It is unclear as to what the moiety is intended to signal for. Moreover, the phrase "signal moiety" is drawn to a moiety which is not described structurally/formulaically/nomenclatorially; but rather by it's mode of action, function or effect requisite to an activity produced. The claim is missing the critical element, which is the

particular or distinct identity of the "signal moiety" on the compound. Defining the variables structurally, formulaically, or nomenclatorially would be a more preferable way to define the subject matter instead of the current functional description. Moreover, the phrase "a reactive group by means of which a signal moiety or a solid surface may be linked to the nucleoside or nucleotide analogue" is indefinite because the recitation of "a reactive group which may (or may not) be able to link to something" is not seen to clearly set forth that which applicants intend as their invention.

It is unclear how claim 7 further limits claim 1, as claim 7 is drawn to a nucleoside analogue comprising the compound according to claim 1, however, the compound of claim 1 is seen to be a nucleoside analogue, thus it is unclear how claim 7 further limits claim 1.

Claim 11 is indefinite wherein the inclusion of parenthetical phrases leaves ambiguity and uncertainty as to whether the contents inside the parenthesis are intended as being that which applicant intends as their invention. Clarity is respectfully requested. Additionally, regarding claim 11, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim 14 is seen to be indefinite wherein the claim does not really set forth any steps in the method. The claim is drawn to a method of detecting a nucleic acid, wherein the only active step is detecting the presence of the reporter moiety, but the claim does not teach how to detect the moiety. Clarity is respectfully requested.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the

explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 15 recites the broad recitation "for detection by spectroscopy", and the claim also recites "especially mass spectroscopy" which is the narrower statement of the range/limitation.

All claims which depend from an indefinite claim are also indefinite. ***Ex parte Cordova, 10 U.S.P.Q. 2d 1949, 1952 (P.T.O. Bd. App. 1989).***

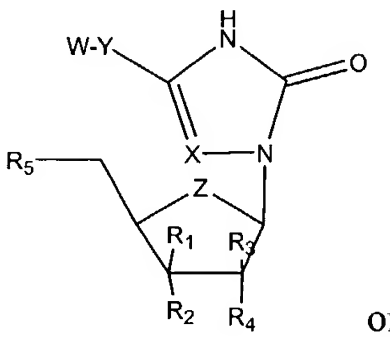
Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

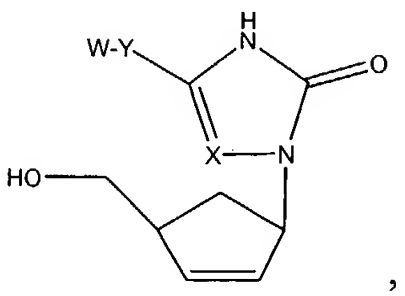
> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States

Claims 1-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Fukuda et al. (reference C1 of IDS).

Claims 1 and 2 are drawn to a compound represented by one of the following structures:



or



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wherein:

X is: either CH or N;

Y is optionally: -CO-, -CONW-, -O-, -S-, -SO-, -SO_2-, -NWCO-, -NW-, or –OCO-;

W is optionally: H, alkyl, aryl, Rp, or –Ln-Rp;

Ln is a linker group;

Rp is a reporter moiety;

Z is: O, S, Se, SO, NW, or CH_2;

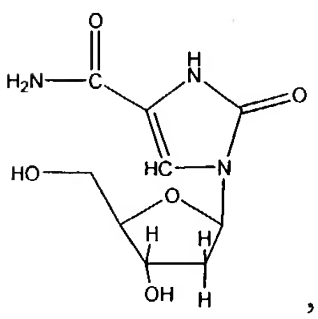
R^1, R^2, R^3, and R^4 are optionally: H, OH, F, NH_2, mono-, di-, or tri-phosphate, -thiophosphate, or –boranophosphate;

or one of R^2 and R^5 is a phosphoramidite or other group for incorporation in a polynucleotide chain, or a reporter moiety.

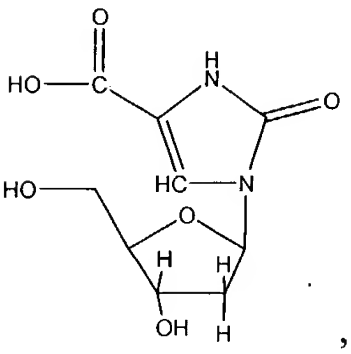
Claim 3 provides that Rp is not in the sugar portion. Claim 4 provides that the linker group is a chain of 1-60 C, N, O, P, and/or S atoms, is rigid or flexible, or is saturated or unsaturated. Claim 5 and 6 provide that the reporter moiety is a signal moiety or a solid surface or a group (NH_2, OH, COOH, $CONH_2$, ONH_2, SH, a thiophosphate, hydrazine, hydrazide, an active ester, aldehyde, or maleimide) which can link to a signal moiety or solid surface. Claim 7 is drawn to a nucleoside comprising the compound of claim 1. Claim 8 is drawn to a nucleotide comprising the

compound of claim 2. Claim 9 limits the R^5 group of claim 8 to triphosphate. Claim 10 is drawn to a polynucleotide chain comprising the nucleoside of claim 7. Claim 11 limits the polynucleotide of claim 10 wherein the sugar is a nucleic acid backbone consisting of sugar-phosphate repeats or modified sugar-phosphate repeats, or a backbone analogue.

Fukuda et al. disclose compounds having the following structure :



, which anticipates the compounds as claimed in the instant application wherein X=CH, Z=O, Y=CO, W=Rp=NH_2, R^1=R^3=R^4=R^5=H, and R^2=OH (see compound 1, page 1572). Fukuda et al. additionally disclose the following compound:



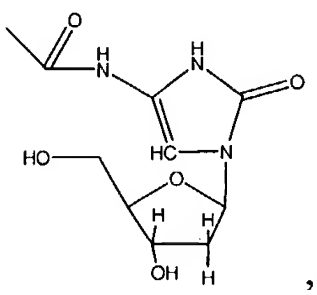
, which anticipates the compounds as claimed in the instant application wherein X=CH, Z=O, Y=CO, W=Rp=OH, R^1=R^3=R^4=H, and R^2=OH (see compound 3, page 1572). Moreover, compound 5 of Fukuda et al. is drawn to an active ester of the compound 3. Additionally, compound 15 (page 1573) comprises a phosphorylated 2'-deoxynucleotide of the compound of formula 1. Additionally, Fukuda et al. disclose that the compounds of formula 15 were applied to solid phase oligomer synthesis by phosphotriester method (page 1573, 1st column, 1st paragraph). Moreover, table I on page 1574 discloses polynucleotides comprising the

nucleoside analogue X (which is analogue 1 as evidenced on page 1573, 2nd column, 1st paragraph).

Claims 1-3, and 5-7 are rejected under 35 U.S.C. 102(a) as being anticipated by Bedu et al. (Document C3 of IDS submitted).

Claims 1-3 and 5-7 are drawn to the compounds as set forth supra.

Bedu et al. disclose compounds having the following structure:



, which anticipates the compounds as claimed in the instant application wherein X=CH, Z=O, Y=NWCO (wherein this W=H), W=alkyl=CH_3, R^1=R^3=R^4=R^5=H, and R^2=Rp=OH (see compound 2a of scheme 3).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

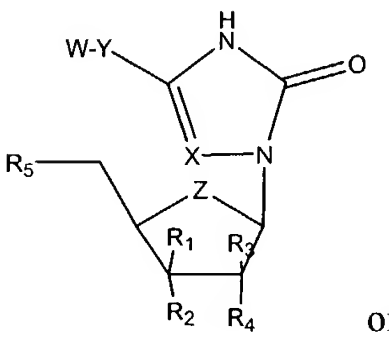
> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

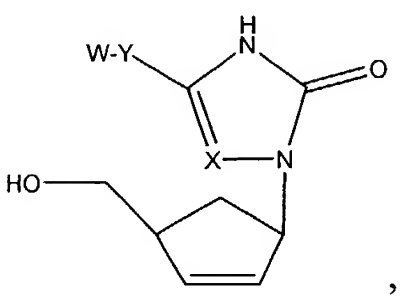
Determining the scope and contents of the prior art.
Ascertaining the differences between the prior art and the claims at issue.
Resolving the level of ordinary skill in the pertinent art.
Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brown et al. (U.S. Patent No. 6,239,159) in view of Fukuda et al. (reference C1 of IDS).

Claims 1 and 2 of the instant application are drawn to a compound represented by one of the following structures:



or



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wherein:

X is: either CH or N;

Y is optionally: -CO-, -CONW-, -O-, -S-, -SO-, -SO_2-, -NWCO-, -NW-, or –OCO-;

W is optionally: H, alkyl, aryl, Rp, or –Ln-Rp;

Ln is a linker group;

Rp is a reporter moiety;

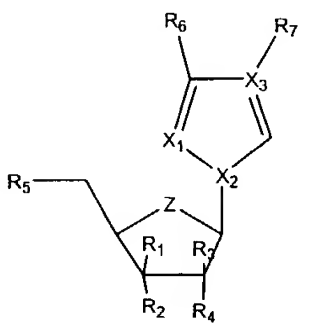
Z is: O, S, Se, SO, NW, or CH_2;

R^1, R^2, R^3, and R^4 are optionally: H, OH, F, NH_2, mono-, di-, or tri-phosphate, -thiophosphate, or –boranophosphate;

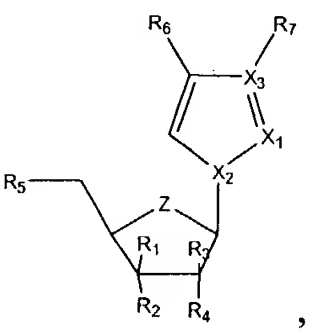
or one of R^2 and R^5 is a phosphoramidite or other group for incorporation in a polynucleotide chain, or a reporter moiety.

Claim 3 provides that Rp is not in the sugar portion. Claim 4 provides that the linker group is a chain of 1-60 C, N, O, P, and/or S atoms, is rigid or flexible, or is saturated or unsaturated. Claim 5 and 6 provide that the reporter moiety is a signal moiety or a solid surface or a group (NH_2, OH, COOH, $CONH_2$, ONH_2, SH, a thiophosphate, hydrazine, hydrazide, an active ester, aldehyde, or maleimide) which can link to a signal moiety or solid surface. Claim 7 is drawn to a nucleoside comprising the compound of claim 1. Claim 8 is drawn to a nucleotide comprising the compound of claim 2. Claim 9 limits the R^5 group of claim 8 to triphosphate. Claim 10 is drawn to a polynucleotide chain comprising the nucleoside of claim 7. Claim 11 limits the polynucleotide of claim 10 wherein the sugar is a nucleic acid backbone consisting of sugar-phosphate repeats or modified sugar-phosphate repeats, or a backbone analogue. Claims 11 and 12 are drawn to chain extension methods comprising reacting the polynucleotide chain of claim 10 with a primer in the presence of a polymerase. Claims 14 and 15 are drawn to methods of detecting a nucleic acid of claim 1 comprising the steps of detecting the presence of the reporter moiety (wherein the reporter is a radioisotope, isotope, signal moiety, or moiety detectable by spectroscopy).

The '159 patent is drawn to nucleosides optionally having the following structure:



or



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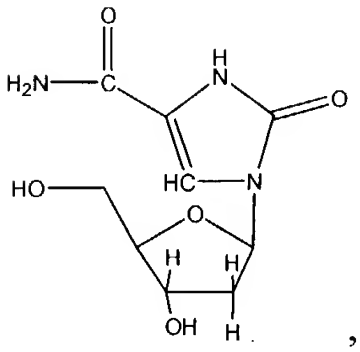
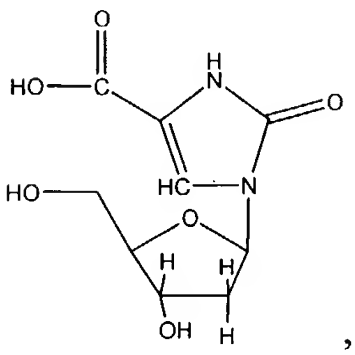
wherein Z, R_1, R_2, R_3, R_4, R_5, R_6, and R_7 are drawn to multiple groups which overlap substantially with the corresponding R-groups of the instant application. X_1, X_2, and X_3 are

optionally C or N. The main structural difference between the compounds above and the compounds as claimed in the instant application is the inclusion of 2 double bonds in the base portion of the nucleoside (between X_3 and X_1 in the second structure, for example). The '159 patent additionally claims that the reporter group can be attached via a linker group (claim 6). Claims 7 and 8 are drawn to polynucleotide chains containing the nucleoside of claim 1 and a signal moiety. Claims 9 and 10 are drawn to chain extension methods comprising reacting the polynucleotide chain of claim 10 with a primer in the presence of a polymerase, for example. Claim 11 is drawn to a method of detecting a nucleic acid of claim 1 comprising the steps using an antibody which binds to the base (which comprises a reporter moiety). What is not specifically taught is the compounds of the instant application, or the use of the compounds of the instant application.

Fukuda et al. disclose compounds having the following structure :



, which falls within the group of compounds claimed in the instant application wherein X=CH, Z=O, Y=CO, W=Rp=NH_2, R^1=R^3=R^4=R^5=H, and R^2=OH (see compound 1, page 1572). Fukuda et al. additionally disclose the following compound:



, which falls within the group of compounds as claimed in the instant application wherein X=CH, Z=O, Y=CO, W=Rp=OH, R^1=R^3=R^4=H, and R^2=OH (see compound 3, page 1572). Moreover, compound 5 of Fukuda et al. is drawn to an active ester of the compound 3. Additionally, compound 15 (page 1573) comprises a phosphorylated 2'-deoxynucleotide of the compound of formula 1. Additionally, Fukuda et al. disclose that the compounds of formula 15 were applied to solid phase oligomer synthesis by phosphotriester method (page 1573, 1st column, 1st paragraph). Moreover, table I on page 1574 discloses polynucleotides comprising the nucleoside analogue X (which is analogue 1 as evidenced on page 1573, 2nd column, 1st paragraph). The compounds of Fukuda were designed to be heterocyclic "lure" bases which, when incorporated into ambiguous positions of oligo-deoxynucleotide probe, were expected to contribute to the stabilization of the duplex by pairing with natural base counterparts (page 1571, 2nd column). Compound 1 of Fukuda et al. is shown to be a common substitute for T and C at the position of redundancy, and are therefor shown to be good analogues for binding to pyrimidine bases (page 1574, second column). Thus, the compounds as claimed in the instant application are known in the art to be art recognized nucleoside analogues.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the nucleoside analogues of Fukuda et al. and add various signal moieties on them for detection in a polynucleotide as in the '159 patent with these references before them. Fukuda et

al. shows that their compounds are indeed effective as nucleoside analogues, and that they bind with pyrimidine bases in duplex DNA sequences. The '159 patent is drawn to compounds with reporter molecules which are to be included into duplex DNA sequences, and then later to be detected via the reporter group, thus it would have been obvious to use the compounds of Fukuda et al. because they were already known to be capable of being incorporated into DNA sequences. Column 2, lines 22-32 of the '159 patent teach that nucleoside analogues are capable of being incorporated into a nucleic acid, and is capable of base-pairing with a nucleotide residue in a complementary chain, and that the analogue may be specific, by pairing with only one nucleotide, or degenerate by pairing with 2 or 3 of the natural bases, or universal, by pairing with each of the natural bases. Fukuda et al. show that their compounds are indeed capable of binding with pyrimidine bases ion a complementary strand of nucleic acid, thus it would have been obvious to use the compounds of Fukuda et al. and tag them as in '159. Moreover, obviousness based on similarity of structure and function entails motivation to make claimed compound in the expectation that compounds similar in structure will have similar properties. Where the prior art compounds essentially bracket the claimed compounds and are known to be effective as well known pesticides, for example, one of ordinary skill in the art would be motivated to make the claimed compounds in searching for new pesticides. See ***In re Payne, 606 F.2d 303, 203 USPQ 245, 254-55 (CCPA 1979).*** As evidenced supra, the compounds of the instant application and the compounds of the '159 patent are indeed very similar in structure, wherein the compounds of '159 have an additional double bond, and have different locations for various overlapping substituents on the ring.

Claims 1-15 of the instant application are seen to be obvious over claims 1-12 of '159, when seen in light of the Fukuda et al. reference.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Traviss C McIntosh whose telephone number is 571-272-0657. The examiner can normally be reached on M-F 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Traviss C. McIntosh
March 31, 2004

James O. Wilson
Supervisory Patent Examiner
Art Unit 1623